CLAIMS

1. A method of identifying a surrogate marker of neuropathic pain in a mammal, comprising:

(a) obtaining a first skin biopsy sample under conditions of neuropathic pain;

(b) obtaining a second skin biopsy sample under conditions of substantially no neuropathic pain;

(c) preparing tissue extracts from the first and the second samples; and

(d) determining an amount of at least one nucleic acid or protein in the tissue extracts;

wherein a difference between the amount of the nucleic acid or the protein in the first sample and the amount of the same nucleic acid or protein in the second sample indicates that the nucleic acid or the protein is a surrogate marker of neuropathic pain.

2. The method of claim 1, wherein the amount of the nucleic acid or the protein in the first sample differs at least 2-fold from the amount of the same nucleic acid or protein in the second sample.

3. The method of claim 1, wherein the first and the second samples are obtained from the same mammal.

4. The method of claim 1, wherein the mammal is a rodent.

5. The method of claim 1, wherein the mammal is a human.

6. The method of claim 1, wherein the nucleic acid or protein is muscle-specific.

7 . A method of evaluating the level of neuropathic pain in a mammal, comprising:

(a) obtaining a first skin biopsy sample under conditions of neuropathic pain;

(b) obtaining a second skin biopsy sample under conditions of substantially no neuropathic pain;

(c) preparing tissue extracts from the first and the second samples; and

(d) determining an amount of at least one nucleic acid or protein in the tissues, the nucleic acid or the protein being a surrogate marker of neuropathic pain;

wherein a difference between the amount of the nucleic acid or the protein in the first sample and the amount of the same nucleic acid or protein in the second sample indicates the level of neuropathic pain.

8. The method of claim 7, wherein the amount of the nucleic acid or the protein in the first sample differs at least 2-fold from the amount of the same nucleic acid or protein in the second sample.

9. The method of claim 7, wherein the first and the second samples are obtained from the same mammal.

10. The method of claim 7, wherein the mammal is a rodent.

11. The method of claim 7, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1-308.

12. The method of claim 7, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1-42.

13. The method of claim 7, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:309-470.

14. The method of claim 7, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:309-333.

15. The method of claim 7, wherein the mammal is a human.

16. The method of claim 7, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:471-630.

17. The method of claim 7, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:471-493.

18. The method of claim 7, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:631-790.

19. The method of claim 7, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:631-653.

20. The method of claim 7, wherein the surrogate marker is muscle-specific.

21. A method of evaluating the effect of a compound or composition on the level of neuropathic pain in a mammal, comprising:

(a) administering the compound or composition to the mammal having neuropathic pain;

(b) obtaining at least one skin biopsy sample from the mammal;

(c) preparing a tissue extract from the skin biopsy sample; and

(d) determining an amount of at least one nucleic acid or protein in the tissue extract, the nucleic acid or the protein being a surrogate marker of neuropathic pain;

wherein a difference in the amount of the nucleic acid or protein determined in step (d) and the amount of the same nucleic acid or protein expressed in the absence of the compound or composition indicates the level of efficacy of the compound or composition on neuropathic pain.

22. The method of claim 21, wherein the amount determined in step (d) that differs at least 2-fold from the amount of the same nucleic acid or protein expressed in the absence of the compound or composition.

23. The method of claim 21 wherein the compound or composition is a neurotrophic agent.

24. The method of claim 21, wherein the neurotrophic agent belongs to the glial cell-derived neurotrophic factor (GDNF) family.

25. The method of claim 21, wherein the neurotrophic agent is artemin.

26. The method of claim 21, wherein the mammal is a rodent.

27. The method of claim 21, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:791-897.

28. The method of claim 21, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:791-814.

29. The method of claim 21, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:898-962.

30. The method of claim 21, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:898-914.

31. The method of claim 21, wherein the mammal is a human.

32. The method of claim 21, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:963-1038.

33. The method of claim 21, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:963-979.

34. The method of claim 21, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1039-1114.

35. The method of claim 21, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1039-1055.

36. The method of claim 21, wherein the nucleic acid or protein is muscle-specific.

37. A method of identifying a biomarker of biological activity of a neurotrophic agent, comprising:

(a) administering the agent to a mammal;

(b) obtaining at least one skin biopsy sample from the mammal;

(c) preparing a tissue extract from the skin biopsy sample; and

(d) determining an amount of at least one nucleic acid or protein in the tissue;

wherein a difference in the amount of the nucleic acid or protein determined in step (d)

and the amount of the same nucleic acid or protein expressed in the absence of the agent indicates that the nucleic acid or the protein is a biomarker of in vivo biological activity of the agent.

38. The method of claim 37, wherein the amount determined in step (d) differs at least 2-fold from the amount of the same nucleic acid or protein expressed in the absence of the agent.

39. The method of claim 37, wherein the neurotrophic agent belongs to the glial cell-derived neurotrophic factor (GDNF) family.

40. The method of claim 37, wherein the neurotrophic agent is artemin.

41. The method of claim 37, wherein the nucleic acid or protein is muscle-specific.

42. A method of evaluating in vivo biological activity of a neurotrophic agent, comprising:

(a) administering the agent to a mammal;

(b) obtaining at least one skin biopsy sample from the mammal;

(c) preparing a tissue extract from the skin biopsy sample; and

(d) determining an amount of at least one nucleic acid or protein in the tissue extract;

wherein a difference in the amount of the nucleic acid or protein determined in step (d)

and the amount of the same nucleic acid or protein expressed in the absence of the agent indicates that the agent is biologically active.

43. The method of claim 42, wherein the amount determined in step (d) differs at least 2-fold from the amount of the same nucleic acid or protein expressed in the absence of the agent.

44. The method of claim 42, wherein the nucleic acid or the protein is a surrogate marker of neuropathic pain.

45. The method of claim 42, wherein the nucleic acid of the protein is a surrogate marker of neurotrophic activity of the agent.

46. The method of claim 42, wherein the neurotrophic agent belongs to the glial cell-derived neurotrophic factor (GDNF) family.

47. The method of claim 42, wherein the neurotrophic agent is artemin.

48. The method of claim 42, wherein the mammal is a rodent.

49. The method of claim 42, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1115-1163.

50. The method of claim 42, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1115-1120.

51. The method of claim 42, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1164-1178.

52. The method of claim 42, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1164-1166.

53. The method of claim 42, wherein the mammal is a human.

54. The method of claim 42, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1179-1207.

55. The method of claim 42, wherein the nucleic acid comprises a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:1179-1182.

56. The method of claim 42, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1208-1236.

57. The method of claim 42, wherein the protein comprises a nonredundant subsequence of any one of amino acid sequences of SEQ ID NOs:1208-1211.

58. The method of claim 42, wherein the nucleic acid or protein is muscle-specific.

59. A method of evaluating the effect of artemin on the level of neuropathic pain in a mammal, comprising:

(a) administering artemin to a mammal having neuropathic pain;

(b) obtaining at least one skin biopsy sample from the mammal;

(c) preparing a tissue extract from the skin biopsy sample; and

(d) determining an amount of at least one nucleic acid in the tissue extract, the nucleic acid comprising a nonredundant subsequence of any one of the nucleotide sequences of SEQ ID NOs:791-814;

wherein a difference in the amount of the nucleic acid or protein determined in step (d) and the amount of the same nucleic acid or protein expressed in the absence of the compound or composition indicates the level of efficacy of the compound or composition on neuropathic pain.

60. The method of claim 59, wherein the amount determined in step (d) that differs at least 2-fold from the amount of the same nucleic acid or protein expressed in the absence of artemin.

61. The method of claim 59, wherein the mammal is a rodent.

62. The method of claim 59, wherein neuropathic pain is caused by a spinal nerve injury.

63. The method of claim 62, comprising obtaining a second skin biopsy sample under conditions of substantially no neuropathic pain.

64. The method of claim 63, wherein the first and the second samples are obtained from the same mammal.

65. The method of claim 64, wherein the first skin biopsy sample is obtained from a first site contralateral to the spinal nerve injury, and a second skin biopsy sample is obtained from a second site ipsilateral to the spinal nerve injury.

66. The method of claim 59, wherein the nucleic acid or protein is muscle-specific.